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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/551,228	09/28/2005	Yves Hatzfeld	BJS-4982-11	3243

23117 7590 09/21/2007

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EXAMINER	
ZHENG, LI	

ART UNIT	PAPER NUMBER
1638	

MAIL DATE	DELIVERY MODE
09/21/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/551,228	HATZFELD ET AL.	
	Examiner	Art Unit	
	Li Zheng	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 July 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *10,11 and 13-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9 and 12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 September 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/28/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-20 are pending.

Election/Restrictions

2. Applicant's elections with traverse of Group III, claim 12, in the reply filed on 3/01/2007 and 6/12/2007 is acknowledged.

Applicants contend that Groups I and III should be rejoined because both groups involve the discovery that modulated expression of a TAD protein results in increased yield such that the method by which this modulation is effected does not affect outcome.

During the examination, it was determined that it would not be an undue burden to search and examine the invention groups I and III together. Groups I and III are therefore rejoined. The examiner, however, maintains the restriction requirement for all other groups.

Applicants are advised that since the restrictions between Groups I and III are withdrawn, if any claim(s) that include(s) the limitation of the examined claims is/are presented in a continuation or divisional application, the claim of the application may be subject to a provisional statutory and/or nonstatutory double patenting rejection over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 no longer apply. MPEP804.01.

Claims 10-11 and 13-20 are withdrawn from consideration for being drawn to non-elected inventions.

Claims 1-9 and 12 are examined on the merits.

The requirement is still deemed proper and is therefore made FINAL.

Specification

3. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01. See, for example, page 3, last paragraph; page 4, 1st paragraph; page 5, 4th paragraph; and page 29, 1st paragraph.

4. The use of the trademark "Gateway®" has been noted in this application (pages 28 and 29). They should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-9 and 12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims 1, 3, 8 and 12, the recitation, "TAD protein" or "TAD encoding nucleic sequence", renders the claims indefinite. The definition of the recitations can be found on page 2 and 3 of the specification. However, according to the definition, TAD protein refers to proteins comprising an ATPase domain derived from any TOB3 like protein. It is unclear what is considered to be a TOB3 like protein. Further it is also unclear what ATPase domain is considered to be derived from the TOB3 like protein. The metes and bounds are not clear.

In claims 1, 3 and 12, the recitation, "homologues", renders the claims indefinite. The definition of the recitations can be found in paragraph bridging pages 4-5 as well as the 2nd paragraph of page 5 of the specification. However, it is unclear which one out of the two definitions should be used to define "homologues". The metes and bounds are not clear.

In claims 1, 3 and 12, the recitation, "derivatives", renders the claims indefinite. The definition of the recitations can be found in last paragraph of page 6 of the specification. However, it is unclear how many substitutions, deletions or additions are allowed and how much sequence similarity needs to be maintained. The metes and bounds are not clear.

In claims 1 and 12, the recitation, "wild type", renders the claims indefinite. It is unclear what is considered to be wild type. The metes and bounds are not clear.

In claim 1, the last step of the method in instant claims is inconsistent with the preamble. The last step only results in modulation of the gene in a plant, whereas the preamble states that the method is for increasing yield of a plant.

Written Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-2, 4, 7-19 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a method for increasing yield of a plant by modulating the expression level of a nucleotide sequence encoding a TAD protein or a homologue, derivative or active fragment thereof or by modulating activity thereof.

The Office interprets that the claims encompass any TAD protein or a homologue, derivative or active fragment thereof.

The specification teaches isolating cDNA clones comprising SEQ ID NO: 1 from tobacco plant (specification, paragraph bridging pages 28-29) and constructing expression vector used for rice transformation (specification, page 29, 2nd paragraph). The specification further teaches that transgenic rice plants (T1 and T2 lines) expressing the expression vector comprising SEQ ID NO: 1 encoding SEQ ID NO: 2 are obtained and evaluated by total seed weight, number of filled seeds and Harvest index (specification, Table 3). The specification also describe how to obtain homologues to SEQ ID NO: 2 by using various bioinformatics software or by hybridization experiment (specification, pages 3-9). The specification also present several known homologues of SEQ ID NO: 2 (specification, page 3, 4th paragraph).

Applicants only describe SEQ ID NO: 2 as a TAD protein and list several putative homologues of SEQ ID NO: 2. Applicants do not describe any active fragment of SEQ ID NO: 2. Further, Applicants also fail to describe any other nucleotide sequence encoding a TAD protein or a homologue, derivative or active fragment thereof. Applicants also do not correlate the function of increasing grain yield in plant with nucleotide sequence other than SEQ ID NO: 1.

The Federal Circuit has recently clarified the application of the written description requirement to inventions in the field of biotechnology. See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). In summary, the court stated that a written description of an invention requires a precise definition, one that defines the structural features of the chemical genus that distinguishes it from other chemical structures. A definition by function does not suffice

to define the genus because it is only an indication of what the gene does, rather than what it is. The court goes on to say, "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus." *See University of California v. Eli Lilly and Co.*, 119 F.3d 1559; 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Applicants fail to describe a representative number of polynucleotide sequences encoding a TAD protein or a homologue, derivative or active fragment thereof. Applicants also do not describe structural features common to the claimed genus. Hence, Applicants fail to meet either prong of the two-prong test set forth by *Eli Lilly*. Since said genus has not been described by specific structural features, the specification fails to provide an adequate written description to support the breath of the claims.

Scope of Enablement

7. Claims 1-9 and 12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for increasing seed yield of a plant by introducing an expression cassette comprising a nucleotide sequence encoding the polypeptide of SEQ ID NO: 2, does not reasonably provide enablement for a method for increasing any kind of yield of a plant by any other means to modulate the expression

level of a nucleotide sequence encoding a TAD protein or a homologue, derivative or active fragment thereof or modulating activity thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The claimed invention is not supported by an enabling disclosure taking into account the *Wands* factors. *In re Wands,* 858/F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). *In re Wands* lists a number of factors for determining whether or not undue experimentation would be required by one skilled in the art to make and/or use the invention. These factors are: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples of the invention, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claim.

The claims are drawn to a method for increasing yield of a plant by modulating the expression level of a nucleotide sequence encoding a TAD protein or a homologue, derivative or active fragment thereof or by modulating activity thereof.

The Office interprets that the claims encompass any means to increase the expression levels of any TAD genes or activity of TAD protein.

The specification teaches isolating cDNA clones comprising SEQ ID NO: 1 from tobacco plant (specification, paragraph bridging pages 28-29) and constructing expression vector used for rice transformation (specification, page 29, 2nd paragraph). The specification further teaches that transgenic rice plants (T1 and T2 lines) expressing the expression vector comprising SEQ ID NO: 1 encoding SEQ ID NO: 2 are

obtained and evaluated by total seed weight, number of filled seeds and Harvest index (specification, Table 3). The result indicates that heterologous expression of SEQ ID NO: 1 in rice plants significantly increases the grain yield of the plants (paragraph bridging pages 32-33). The specification further propose to apply the method in maize (specification, page 33, 2nd paragraph).

First, there is no evidence that expression of SEQ ID NO: 1 would increase the yield of any tissue other than the grain.

Further, the specification does not demonstrate which endogenous orthologous gene(s) of SEQ ID NO: 2 are affected due to the heterologous expression of SEQ ID NO: 1. The specification does not demonstrate whether the phenotype caused by heterologous expression of SEQ ID NO: 1 is due to an increase or a decrease of activity of the endogenous orthologous gene(s) of SEQ ID NO: 2. Therefore, the specification does not provide guidance on which rice gene(s) to be modulated and how to modulate the genes to achieve the same phenotype. Without such guidance, undue experimentation would be required for a person skilled in the art to identify orthologous gene in all plant and further develop recombinant means or chemical means to modulate the expression to obtain the same phenotype.

Further still, the specification fails to provide guidance on how to obtain a nucleotide sequence encoding a TAD protein or a homologue, derivative or active fragment thereof. The specification does not teach any other active fragment of SEQ ID NO: 1 except for SEQ ID NO: 1 itself. The specification only lists several known putative homologues of SEQ ID NO: 2 determined by sequence similarity and only

provides general tools such as blast search or hybridization to identify homologous gene by sequence homology. However the claims encompass a genus of nucleotide sequences or polypeptide sequences, most of which are not exemplified. Further, even if the homolgous genes are obtained, the specification teach that ATPases Associated with variety of cellular Activities (AAA) play a role in different cellular processes including cell cycle, organelle synthesis, mitochondrial functioning, vesicle transport, protein turnover, regulation of the cytoskeleton and intracellular motility; that AAA proteins may represent a broad class of mechanoenzymes that have evolved unique ways of using a fundamentally similar conformational change in many different biological settings, but the basis of interaction with their target proteins is still a matter of speculation (specification , page 1, 2nd paragraph). Therefore a homologous gene obtained by sequence homology may well be a member of the family functions in a complete different pathway.

Transforming plants with heterologous genes that are involved in plant development produce unpredictable results. Kano-Murakami et al (1993, FEBS 334:365-368) teach introducing the *Oryza sativa* homeobox 1 (OSH1) gene into tobacco. OSH1 is a rice homologue of the *Knotted-1* homeobox gene from maize and would be encompassed by Applicant's broad claim language. Kano-Murakami et al teach transgenic tobacco plants comprising the OSH1 gene display a "range of phenotypes which include abnormalities in leaf and petal shape as well as stem height and number" (page 365, right column, 1st paragraph).

Further, the specification does not teach other ways to up-regulate the expression of TAD protein. However, genes can be regulated in many other ways that are not enabled by the specification. For example, over-expression of a gene can be achieved by down-regulating the negative regulators of the gene. Likewise, up-regulation of a gene can be achieved by up-regulating the positive regulators of the gene. The transcriptional factors could be among those regulators. Still further the protein activity can also be modulated by many other ways such as by posttranslational modification or by inhibition of the inhibitors. The specification does not provide any guidance on what kind of modification can be made to up-regulate the activity of the protein. The specification does not provide guidance on the positive or negative transcriptional factors for those genes.

Therefore, undue experimentation would be required by one skilled in the art to clone and characterize genes encoding TAD proteins from other plants by, for example, either hybridizing with unspecified probes from maize homologous genes or PCR amplification using unspecified primers, to make expression cassette comprising the isolated genes, to transform the resulting expression vectors into plants and to assay yield increase, if any, of the transgenic seeds. See *Genentech Inc. v. Novo Nordisk,* A/S (CA FC) 42 USPQ2d 1001 (Fed. Cir. 1997), which teaches that "the specification, not the knowledge of one skilled in the art" must supply the enabling aspects of the invention.

Therefore, given the claim breadth, lack of further guidance and additional working example, unpredictability of the art, undue experimentation would be required for a person skilled in the art to practice the invention.

Claim Rejections - 35 USC § 102

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

8. Claims 1-2 and 4-9 rejected under 35 U.S.C. 102(b) as being anticipated by Lorenzo et al. (Jan. 2002, Plant Cell Physiol. 43:27-34).

The claims are drawn to a method for increasing yield of a plant by modulating the expression level of a nucleotide sequence encoding a TAD protein or a homologue, derivative or active fragment thereof or by modulating activity thereof; or wherein said modulation is affected by chemical means; or wherein said increased yield comprises increased seed yield or an increase in the number of filled seeds, total seed weigh or Harvest Index; or wherein said modulated expression is overexpression.

Because the indefiniteness of "TAD protein" as discussed above, the Office interprets TAD protein to encompass any AAA protein.

Lorenzo et al. teach that the expression of FsA1 gene, a member of AAA family, is induced in beechnuts seeds by applying gibberelic acid (abstract). Although Lorenzo et al. do not teach such modulation could increase seeds yield, the reference teaches the same steps. See *Integra LifeSciences I Ltd. V. Merck KGaA* 50 USPQ2d 1846, 1850 (DC SCalif 1999), which teaches that where the prior art teaches all of the required steps to practice the claimed method and no additional manipulation is required to produce the claimed result, then the prior art anticipates the claimed method. Given that the office interprets FsA1 to be a TAD protein or a homologue, derivative or active fragment thereof for the reasons states above, Lorenzo et al. anticipate the claimed invention.

9. Claims 1-3, 8-9 and 12 are rejected under 35 U.S.C. 102(e) as being anticipated by Kwart et al. (2004, U.S. Patent Application Publication No. 2004/0168214).

The claims are drawn to a method for increasing yield of a plant by modulating the expression level of a nucleotide sequence encoding a TAD protein or a homologue, derivative or active fragment thereof or by modulating activity thereof; or wherein the nucleotide sequence is from a plant; or wherein said modulation is overexpression.

Because the indefiniteness of "TAD protein" as discussed above, the Office interprets TAD protein to encompass a proton ATPase, PHA2,.

Kwart et al. teach that expression of a cDNA from potato encoding a proton ATPase, PHA2, in plant increases the yield (paragraphs [0110]-[0116]; also claim) The Office interprets PHA2 to be a TAD protein or a homologue, derivative or active

fragment thereof for the reasons stated above. Therefore, the reference teaches all the limitation set forth by the instant claims.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Li Zheng whose telephone number is 571-272-8031. The examiner can normally be reached on Monday through Friday 9:00 AM - 5:30 PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg can be reached on 571-272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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